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Brief Report

Information about chemotherapy-associated cognitive problems contributes to cognitive problems in cancer patients

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Abstract

***Objective*: Although increasing attention is directed at identifying biological mechanisms underlying cognitive changes observed in cancer patients without central nervous system disease following chemotherapy, psychological factors that can contribute to these cognitive changes are much less studied.**

***Methods*: In an online experiment, the influence of informing patients about the association between cognitive problems and chemotherapy on self-reported cognitive functioning and neuropsychological test performance was investigated.**

***Results*: Cancer patients treated with chemotherapy ($n = 150$) reported higher levels of cognitive complaints after receiving such information ($M = 21.20$) than without such information ($M = 18.98$; $p = 0.032$). No difference was found for patients without (a history of) chemotherapy (n = 86; $M = 18.85$ vs. 20.08; NS). A similar interaction pattern was observed on a word-learning test. Patients treated with chemotherapy recalled fewer words after being informed about the association between cognitive problems and chemotherapy ($M = 24.44$) than without such information ($M = 27.63$; $p = 0.010$). No difference was found for patients not treated with chemotherapy ($M = 26.35$ vs. 25.38; NS).**

***Conclusion*: Patient information may induce a stereotype threat, which affects self-reported cognitive function and neuropsychological test performance in cancer patients for whom this information is relevant.**

Keywords: cancer; oncology; cognitive complaints; neuropsychological test performance; priming; chemotherapy

Introduction

Neuropsychological studies show that cognitive changes may occur in a subset of cancer patients following chemotherapy. Insight into mechanisms that underlie these cognitive changes improves, but much needs to be learned. Most current studies are rooted in biology, unraveling the complex neural basis of cognitive changes associated with chemotherapy [1–4]. Less is known about relevant psychological variables. Although studies show that the reporting of cognitive complaints by patients is often related to symptoms of anxiety and depression and to general complaints such as fatigue, psychological factors tend to show only weak associations with cognitive problems as measured by neuropsychological tests [5–7].

A thus far overlooked explanation that can contribute to the occurrence of cognitive problems is the extent to which a patient is (made) aware of the possibility of cognitive problems following chemotherapy. The proposition that mere awareness about potential side effects can increase the occurrence of side effects draws on a large body of evidence from social psychological and health psychology researches on the concept of stereotype threat, proposing that the activation of stereotypical information—such as 'chemotherapy causes cognitive problems'—can have a powerful effect on cognitive performance [8,9]. Famous lab studies on prejudice have shown that informing women that 'women are bad at math' lowers their scores on a math test [10]. Likewise, African Americans primed with racial stereotypes consistently obtained lower scores on IQ tests [11]. These priming effects are proposed to occur because negative stereotypes trigger concerns of being evaluated based on this stereotype, which in turn, disrupt performance, thereby creating a self-fulfilling prophecy.

Why is this predicament relevant for research on cognitive problems following chemotherapy? The effects of stereotypical information may become stronger with repeated exposure. Hence, mere information about chemotherapy-related side effects, for

instance provided by physicians or by patient groups, may increase cognitive complaints and may depress cognitive test performance. Recent findings showed that providing breast cancer patients in a hospital waiting room with stereotypical information about the relation between chemotherapy and cognitive problems increased the expression of cognitive complaints, in particular among patients with prior awareness of this relation but without chemotherapy experience [12]. The present study extends these findings by examining (i) whether priming also influences actual cognitive performance as assessed by neuropsychological testing and (ii) whether stereotypical information also functions as a threat when applied to patients outside the active hospital setting.

Methods

We applied a 2×2 factorial between-subjects design in this study. Patients were recruited via cancer websites, where they were asked to participate in an online study 'on the effects of cancer therapies on individual patients'. Following the general opening text, the participants were randomly assigned—by computer—to one of two experimental conditions; half of the patients received the introduction that 'some patients treated with chemotherapy experience cognitive problems' (the priming condition). The other half of the patients received a neutral introduction (control condition). Self-reported cognitive complaints were measured with the subscales 'absent-mindedness' and 'names and words' of the Dutch version of the Cognitive Failure Questionnaire [13,14]. These subscales consist of 10 items, which are rated on a five-point scale (maximum score is 40). Higher scores denote more self-reported complaints. Cognitive performance was assessed with the Groningen Fifteen Words Test (short version), a learning and memory test commonly used in the Netherlands, originally developed by Rey [15,16]. This test was adapted for online use according to a procedure developed at Rutgers-Newark. In this test, 15 words are successively presented, and patients are asked to rate each word as positive or negative. In a subsequent screen, patients are asked to recall as many words as possible. This procedure is repeated three times. Correctly recalled words are summed across trials; higher scores denote higher levels of cognitive performance (maximum score is 45). Affect was assessed with five items from the Positive and Negative Affect Schedule [17]. The patients had to indicate on a 5-point Likert scale the extent to which they experienced a specific emotion at this moment; higher scores denote more positive affect. Finally, the patients were asked whether they had pre-existing knowledge (prior to the experiment) about the fact a subgroup of patients experience cognitive problems during and following cancer diagnosis and treatment and indicate relevant medical details, for example, whether they were currently or previously treated with chemotherapy. The patients were also asked if they were a member of a cancer patient organization. The average time to complete the online experiment was about 20 min.

Statistical analyses

The findings were analyzed with the statistical package SPSS Version 17.0 (SPSS, Inc, Chicago, IL, USA) using 2×2 analyses of variance with primed introduction (yes, no) and firsthand chemotherapy experience (yes, no) as between-subjects factors. Assumption of equal variance was assessed with Levene's test. Simple effects analyses were used to further examine significant interaction effects. Effect sizes were calculated with partial eta square.

Results

A total of 236 cancer patients were included in the study. Patients who were currently or previously treated with chemotherapy were assigned to the 'chemotherapy' group ($n = 150$); the remaining patients were assigned to a group without (a history of) chemotherapy ($n = 86$). The experimental and control groups were equally distributed with regard to other demographic and clinical variables (Table 1). Levene's test confirmed the assumption of equal variance across conditions. A significant interaction between priming and firsthand chemotherapy experience was observed on the Cognitive Failure Questionnaire ($F(1,\ 232) = 4.01,\ p = 0.046,\ \eta_p{}^2 = 0.02$). Patients with (a history of) chemotherapy reported higher levels of cognitive complaints after receiving a prime ($M = 21.20$) than without prime ($M = 18.98$; $p = 0.032$). No such difference was found for the no-chemotherapy patients ($M = 18.85$ vs. 20.08, respectively; NS) (Table 2). A similar interaction pattern was observed on the Fifteen Words Test ($F(1, 232) = 4.04$, $p = 0.046$, $\eta_p{}^2 = 0.02$). The patients with chemotherapy learned fewer words after receiving a prime ($M = 24.44$) than without prime ($M = 27.63$; $p = 0.010$). No such difference was found for the no-chemotherapy patients ($M = 26.35$ vs. 25.38, respectively; NS) (Table 2). Priming and firsthand experience with chemotherapy had no effect on affect. Pre-existing knowledge of the relation between chemotherapy and cognitive problems had no effect on self-reported cognitive complaints and neuropsychological test performance (general knowledge levels were very high, i.e., most participants knew about the relationship between chemotherapy and cognitive complaints; Table 1).

Discussion

Our findings show that mere information about the association between cognitive problems and chemotherapy can increase the reporting of cognitive problems

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Table 1. Distribution of demographic and clinical characteristics across groups

	Control group (no priming condition) $N = 120$	Experimental group (priming condition) $N = 116$	p-value
Age, mean (SD)	48.3 (10.3)	48.6 (10.2)	0.83
Experience with CT (%) (n/N)[a]	56.7 (68/120)	70.7 (82/116)	0.03[b]
Time since diagnose, years (SD)	4.2 (3.2)	4.5 (4.2)	0.58
Member patient group (%) (n/N)	42.0 (47/112)	44.6 (50/112)	0.79
Breast cancer diagnosis (%) (n/N)	62.5 (75/120)	68.1 (79/116)	0.41
Pre-existing knowledge[b] (%) (n/N)	78.4 (91/116)	73.5 (93/113)	0.44
Working			
No (%) (n/N)	40.5 (47/116)	34.8 (39/112)	
Yes (%) (n/N)	13.8 (16/116)	15.2 (17/112)	
Temporarily stopped (%) (n/N)	45.7 (53/116)	50.0 (56/112)	0.68
Gender			
Male (%) (n/N)	8.6 (10/116)	11.6 (13/112)	
Female (%) (n/N)	91.4 (106/116)	88.4 (99/112)	0.51
Education			
Low (%) (n/N)	24.6 (28/114)	30.6 (34/111)	
Moderate (%) (n/N)	57.9 (66/114)	57.7 (64/111)	
High (%) (n/N)	17.5 (20/114)	11.7 (13/111)	0.36

Variations in N across demographic and patient characteristics due to missing values.
SD, standard deviation; CT, chemotherapy.
[a]CT, past or current chemotherapy (six patients were currently receiving chemotherapy).
[b]Pre-existing knowledge on relation between cancer treatment and cognitive problems.

Table 2. Mean scores (standard deviation) of self-reported cognitive complaints and cognitive performance as a function of experience with chemotherapy and experimental condition (priming versus no priming)

	Experimental group (priming) $N = 116$	Control group (no priming) $N = 120$	p-value	η_p^2
Cognitive complaints (CFQ)				
CT [a]	21.20 (6.4)	18.98 (6.7)	0.032	0.02
No CT	18.85 (6.1)	20.08 (5.3)	0.375	0.003
Cognitive performance (Groningen Fifteen Words Test)				
CT [a]	24.44 (8.3)	27.63 (7.1)	0.010	0.03
No CT	26.35 (6.7)	25.38 (7.3)	0.561	0.001

CFQ, Cognitive Failure Questionnaire; CT, chemotherapy.
[a]CT, past or current chemotherapy (six patients were currently receiving chemotherapy).

and can depress cognitive performance, in particular for patients who have experience with chemotherapy. These findings are in line with psychological findings that stereotype priming predominantly affects cognitive performance of relevant target groups [8–11], although recent evidence suggests that effects on complaint reporting may extend to other patient groups [12].

Clearly, more research is needed to identify groups and group members susceptible to stereotype priming. Specifically, the relationship among priming, previous knowledge, and experience with chemotherapy appears worthwhile examining further. Although in the present study, priming affected the reporting of cognitive complaints and cognitive test scores mainly for patients with a history of chemotherapy, a previous study reported opposite findings on cognitive complaints, that is, that priming increased cognitive complaints mostly for patients without a history of chemotherapy [12]. It may be that previous knowledge regarding the relationship between chemotherapy and cognitive complaints is a prerequisite for priming effects to occur among specific target audiences; in the present study, knowledge levels were very high, whereas in the previous study, only half of the patients knew about the relationship between chemotherapy and cognitive complaints. Alternatively, it may be that previously observed findings were caused by a ceiling effect. This explanation is corroborated by the fact that a history of chemotherapy had a main effect on complaint reporting in the previous study but not in the present study. Clearly, this issue and other potential confounds need to be examined further.

One potential limitation of online studies, like the current study, is that there is no method for confirming that respondents are actually cancer patients. The fact that we posted the questionnaire on Internet sites for cancer patients diminishes this risk considerably. Nevertheless, future studies should benefit from including offline settings to verify patient demographics and to verify whether participants completed the cognitive measures on their own, without the use of cues.

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Our research should be regarded as a first indication that psychological concepts like stereotype threat may play a contributory role in the occurrence of cognitive problems. Future studies should examine the duration of this effect and test whether frequent exposure to stereotypical information increases its impact by inducing chronic activation of stereotypical information, as may be expected from related research [8,9]. This is particularly important considering that public awareness of the relation between cancer treatment and cognition is growing [18]. Increased awareness may not only amplify the reporting and occurrence of cognitive problems for groups at risk, it may also amplify patients' requests for effective interventions. Currently, empirically supported neuropsychological rehabilitation programs for cancer patients are still limited but increasingly studied [19,20]. Social psychological research suggests that teaching target groups about stereotype threat or providing them with positive affirmations may attenuate the negative effects of stereotype threat [21,22]. Mere information may cause and undo the negative effects of stereotype activation. Future studies should not only focus to further refine our understanding of the psychological processes that can hamper cognitive functioning and on specific risk groups, but also on what can be done to reduce or prevent the occurrence of cognitive problems from a social psychological point of view.

Conflict of interest

The authors declare no conflict of interest.

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